

Notice of Allowability

Application No.

09/778,672

Examiner

Q. Janice Li, M.D.

Applicant(s)

CHING-HSAING ET AL.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/26/05.
2. ☒ The allowed claim(s) is/are 24-33,35-39 and 41-49.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 10/21/03; 1/28/05
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Q. JANICE LI, M.D. Q. Janice Li, M.D.
PRIMARY EXAMINER Primary Examiner
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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/26/05 has been entered.

No claim has been amended. Claims 24-33, 35-39, 41-49 are pending and under current examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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The prior rejection of Claims 24-33, 35-39, and 41-49 under 35 U.S.C. 103(a) as being unpatentable over *Hsu et al* (US 5,958,891) and *Janeway Jr.* (Immunobiology, 1999), in view of *Pouwels et al* (Intl J Food Microbial 1998;41:155-67) and *Medaglini et al* (PNAS 1995;92:6868-72, IDS/AI), is withdrawn for reasons set forth below in the section of an examiner's statement of reasons for allowance.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jianming Hao on December 5, 2005.

The claims have been amended as follows:

In claim 24, --the-- was inserted in place of "a" before "subject" in line 3; -- thereby-- was inserted before "expressing" in line 7; -- said-- was inserted in place of the second phrase "the non-pathogenic, Gram-positive" bridging lines 7 and 8; and -- an -- was inserted before "allergen-specific in line 9.

In claim 33, the first phrase "of claim" was deleted in line 1.

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In claim 36, --the-- was inserted in place of "a" before "subject" in line 3; -- thereby-- was inserted before "expressing" in line 5; and -- an -- was inserted before "allergen-specific in line 6.

In claim 39, --belongs to -- was inserted in place of "is of" in line 1.

In claim 41, -- 39 -- was inserted in place of "40".

In claim 43, --a-- was inserted in place of "an" in line 2; --the-- was inserted in place of "a" before "subject" in line 3; -- thereby-- was inserted before "expressing" in line 7; -- said-- was inserted in place of the phrase "the non-pathogenic, Gram-positive" in line 8; and -- an -- was inserted before "aeroallergen-specific" in line 9.

In claim 44, -- alleviating -- was inserted in place of "relieving" in line 1; --the-- was inserted in place of "a" before "subject" in line 3; -- thereby-- was inserted before "expressing" in line 5; and -- alleviate -- was inserted in place of "relieve" in line 6.

In claim 45, --belongs to -- was inserted in place of "is of" in line 1.

The following is an examiner's statement of reasons for allowance:

Upon further search and careful review of the prior art of record, and numerous communications on record, the prior rejection of Claims 24-33, 35-39, and 41-49 under

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35 U.S.C. 103(a) as being unpatentable over *Hsu et al* (US 5,958,891) and *Janeway Jr.* (Immunobiology, 1999), in view of *Pouwels et al* (Intl J Food Microbial 1998;41:155-67) and *Medaglini et al* (PNAS 1995;92:6868-72, IDS/AI), is withdrawn because the combined teachings fail to teach or suggest a reasonable expectation of success on suppressing IgE production in an allergic response induced by an aeroallergen expressed by a non-pathogenic, Gram-positive bacterium via oral administration.

It is noted that *Hsu et al* '891 patent teach suppressing IgE production/allergic asthma by intramuscular injection of a non-viral eukaryotic plasmid expression vector. Although *Pouwels et al* and *Medaglini et al* teach the desirability of using the oral commensal bacterium (an prokaryotic vector) as a vaccine carrier, they fail to teach the influence of the subsequent immune response on IgE production, the cited art of record only teach the effect of said immune response on IgG and IgA production. Given the differences in the type of allergens, in the type of carriers, in the underlying mechanisms of allergen processing and presentation when expressed by said bacterium, in the route of administration, and the unpredictability of the overall clinical effect in an experimental asthma model, the claimed method is considered novel and non-obvious in light of the state of the art coupled with the instant disclosure as a whole.

The above conclusion is reinforced by a new-found prior art, wherein *Jahn-Schmid et al* (Immunotechnol 1996;2:103-13) investigated suppressing allergic response using a fusion protein between a gram-positive bacterial surface layer (S-layer) protein and an allergen. Interestingly, *Jahn-Schmid et al* demonstrated the adjuvant effect of the surface layer, i.e. the allergen-S-layer fusion protein enhanced

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IgG production and T cell response in an allergen-specific manner (e.g. section 3.2.2). Again the publication is silent concerning IgE production in a mouse model or how the allergen-specific immune response influences clinical outcome on allergy. In fact, *Jahn-Schmid et al* teach the allergen fusion protein would bind to IgE antibody in an *in vitro* assay, which raises a reasonable doubt as to whether the allergen expressed by a non-pathogenic, gram-positive bacterium would enhance or suppress IgE production in a subject upon oral administration. Accordingly, even when combined with the *Hsu* '891 patent, the claimed method is considered novel and non-obvious in light of the state of the art.

It is noted that US Patent 6,737,521 contemplates delivery and expression of a hybrid protein on the surface of a non-pathogenic, gram-positive bacterium, wherein the protein may be a dust allergen (column 13, lines 6-9). However, the '521 patent fails to teach the practical means of vaccination, nor a reasonable expectation of success on suppressing IgE production, and on suppressing an airway allergic response. Given the variations in regulating an allergic response concerning the type of allergens, the type of carriers, the underlying mechanisms of allergen processing and presentation when expressed by said bacterium, the route of carrier administration, and the unpredictability of the overall clinical effect in an experimental asthma model, even when combined with the *Hsu et al* '891 patent, the claimed method is considered novel and non-obvious in light of the state of the art coupled with the instant disclosure as a whole.

Conclusion

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Claims 24-33, 35-39, 41-49 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

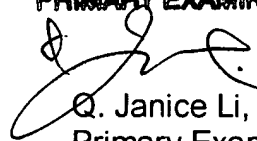
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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

**Q. JANICE LI, M.D.
PRIMARY EXAMINER**



Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL

December 12, 2005